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SIM & MCBURNEY
330 UNIVERSITY AVENUE
6TH FLOOR
TORONTO, ON M5G 1R7
CANADA

EXAMINER	
HAMA, JOANNE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 01/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,569	BRUNHAM, ROBERT C.	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *1-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/21/02* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/16/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

This Application is a 371 of PCT/CA00/01097, filed September 21, 2000, which is a CIP of 09/401,780, filed September 22, 1999, now U.S. Patent 6,632,663.

Claims 1-23 are pending.

Election/Restrictions

Applicant's election without traverse of Group II, claims 12-23 in the reply filed on December 1, 2004 is acknowledged.

Claims 1-11 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on December 1, 2004.

Claims 12-23 are under consideration in this Office Action.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

It is also noted that the IDS contains multiple typographical errors in the titles (for example, #29 and #32). However, based on the references supplied and other information in the citation, the IDS has been fully considered.

Specification

The abstract of the disclosure is objected to because it should be submitted on a separate sheet of paper and not as a duplicate of the coversheet of the PCT. Correction is required. See MPEP § 608.01(b).

The nucleotide sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

Appropriate correction is required.

The absence of proper sequence listing did not preclude the examination on the merits however, for a complete response to this office action, applicant must submit the required material for sequence compliance.

Claims 16 and 20 and the specification refer to sequences. They have been indicated by SEQ ID NOs. However, no computer readable format (CRF), paper copy of the sequence, and statement that the two are the same have been provided.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 12-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inducing an immune response, does not reasonably provide enablement for a protective immune response induced by a vaccine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 12-21 are to a method of using a gene encoding a serine-threonine kinase (STK) of a strain of *Chlamydia* or a fragment of said STK that generates an STK-specific immune response to produce an immune response in a host. Claim 22 is to a method of producing a vaccine for protection of a host against disease caused by infection with a strain of *Chlamydia*. Claim 23 is to a vaccine produced by the method claimed in claim 22.

The Examiner has considered claims 12-21 in two ways. First, the claims can be read to encompass a method wherein an immune response is activated in a host. This is interpreted simply as the host generating antibodies against a foreign antigen. This method is well known in the art and will be discussed further in the 103 rejection. Second, claims 12-21 can be read with the scope wherein the method of generating an immune response also confers protection of a host against disease caused by infection with a strain of *Chlamydia*. In this case, claims 12-21 are also read in mind with claims

22-23. This second situation is encompassed by the claims and its consideration raises issues of enablement.

The specification teaches that a vector comprising a nucleotide sequence encoding a serine-threonine kinase from the *C. trachomatis* mouse pneumonitis strain (MoPn) (page 5, first paragraph) was cloned into a eukaryotic expression plasmid (page 10, line 19-21). The mice were immunized intramuscularly and intranasally with plasmid DNA at 0, 2, and 4 weeks (page 11, lines 13-15). 14 days after the last immunization, mice were challenged intranasally with $2x10^3$ IFU of *C. trachomatis* MoPn EB (page 11, lines 20-21). 10 days after infection, mice were sacrificed and MoPn growth in lung was analyzed by quantitative tissue culture (page 4, lines 23-27). The results are illustrated in Figure 1B. Figure 1B teaches that there are reduced levels of viral load when the mice were injected with STK plasmid, as compared to mice injected with saline or with empty vector. However, reduced levels of virus do not demonstrate that the mice are protected from disease cause by infection with a strain of *Chlamydia*. The data indicates that there is decrease load; however, the pretreatment for expression of STK did not provide a prophylactic and protective effect as would be required by a vaccine. Since the specification does not teach that the vaccine eliminates viral load, the specification does not teach that the STK DNA construct provided immunity of the mice from *Chlamydia*, nor does it enable a method for using the construct. Subsequently, the vaccine is not enabled. Additionally, because the specification does not enable a skilled artisan to use the STK DNA construct in mice to confer immunity, the claims, which broadly encompass any animal host (including humans, claim 21), are not enabled.

The claims also broadly encompass protection from any strain or any immunotype of *Chlamydia*. However, because the specification has not enabled a skilled artisan to protect a host from *Chlamydia* described in the instant specification, a skilled artisan cannot predictably extrapolate how to protect a host from any strain or immunotype of *Chlamydia*.

At the time of filing, many skilled artisans were trying to find a vaccine for *Chlamydia*. Major outer-membrane protein (MOMP) was of particular interest since theoretically, an immune response of a vaccinated host could be readily mounted against an exposed, cell-surface expressed protein and thus would confer immunity of the host from *Chlamydia*. However, work by skilled artisans demonstrates that using partial and full length MOMP did not confer immunity on animal hosts against *Chlamydia*. For example, Su et al. (1995, Vaccine, 13: 1023-1032, see IDS) teach that even after mice were given two booster immunizations subcutaneously with alum-adsorbed peptide at 30 day intervals (see Materials and Methods, paragraph under "Immunization and sample collection"), and were shown to express anti-chlamyidal antibody (page 1025, second column, paragraph under, "Isotype of chlamydial specific antibodies in sera and vaginal washes following immunization with peptide A8-VDIV"), the mice were shown to have no protection from *Chlamydia* after *Chlamydia* challenge. In the 10 ID_{50} challenge group, 80% of the controls were infected compared to a 50% infection rate in vaccinated mice. The incidence of infection in control animals challenged with 10^2 ID_{50} was 100% compared to an 80% infection rate in vaccinated mice. There was no difference in the incidence of infection between vaccinated and

control mice challenged with 10^3 ID_{50} (page 1028, column 1, paragraph under "Challenge experiments" to second column, lines 1-9). In another example, Batteiger et al. (1993, Journal of General Microbiol. 139: 2965-2972) teach that full length (39kDa) MOMP (page 2966, second column, second paragraph under "*Chlamydiae* and protein purification," line 1) was used to immunize guinea pigs (page 2966, second column, under "Experimental animals, immunizations, and challenge infection"). Following immunization, the guinea pigs were examined for immune response by Western blot analysis (page 2967, second column, under "immune response of immunized guinea pigs"; see also figure 1b and Table 2). Following challenge with *Chlamydia*, the animals were examined for protection from *Chlamydia*. Batteiger et al. teach that no protection was observed despite the immune responses (page 2969, second column, paragraph under "Response to challenge infection").

While these studies teach that despite targeting a likely protein candidate for generating an immunity against *Chlaymidia* was unsuccessful, the motivation to carry out the study was clear. Skilled artisans were hoping to invoke an immune response in a vaccinated animal, and thus prevent infection of *Chlamydia*. This would have been achieved by mounting a response to a chlamydial protein that was readily accessible to a host's antibody. In the instant application, the specification teaches that a protein that is expressed within *Chlamydia* to be used as the antigen. Nothing in the specification teaches what the advantage is of using an internal protein, nor does the specification teach what advantage using STK has over any other chlamydial protein in conferring immunity against *Chlamydia*.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alberts et al. (1994, Molecular Biology of the Cell, Third Edition, Garland Publishing: New York, page 1195), in view of Su et al. (1995, Vaccine, 13: 1023-1032, see IDS), Stephens et al. (1998, Science, 282: 754-759, see IDS; see also NCBI nucleotide printout, *Chlamydia trachomatis* D/UW-3/Cs section 15 of 87 of the complete genome, gi number: 3328545, page 1 bottom to 2 top) and Pardoll and Beckerieg (1995, Immunity, 3:165-169, see IDS).

Claims 12-21 are to a method of using a gene encoding a serine-threonine kinase (STK) of a strain of *Chalmydia* or a fragment of said STK that generates an STK-specific immune response. "Specific immune response" has been interpreted to mean generation of antibodies. At the time of filing, the art has shown that skilled artisans were actively trying to induce immunity to *Chlamyida* in host animals. In one example, Su et al. (1995, Vaccine, 13: 1023-1032, see IDS) teach that mice generated antibodies against *Chlamydia* MOMP (page 1025, second column, paragraph under "Isotype of chlamydial specific antibodies in sera and vaginal washes following immunization with peptide A8-VDIV"), following subcutaneous immunization with MOMP peptide, A8-VDIV

(page 1024, paragraph under "Immunization and sample collection"). This example demonstrates one indicator that the skilled artisan used to determine whether an immune response was invoked was to check the host animal's sera for antibodies against the target protein.

Alberts et al. teach that, "almost any macromolecule, as long as it is foreign to the recipient, can induce an immune response; any substance capable of eliciting an immune response is referred to as an antigen (*anti*body *gen*erator)." While Alberts et al. teach that most any macromolecule can generate an immune response, they do not teach the amino acid sequence of *Chlamydia* STK.

Stephens et al. teach the genome sequence of *Chlamyida trachomatis*. Stephens et al. also teach the amino acid sequence of *Chlamydia* STK (see bottom page 1 to top of page 2 of NCBI printout). While Stephens et al. do not demonstrate a one-to-one relationship between the amino acid sequence and the corresponding nucleotide sequence, an artisan of ordinary skill can reverse translate the protein sequence to a nucleotide sequence and obtain a nucleotide sequence same as that of SEQ ID NO. 1. It was also well known at the time of filing that nucleotides encoding proteins could be put into an expression vector and introduced to an animal host. Pardoll and Beckerieg teach that it is well established in the art that injection of naked DNA through any number of routes reproducibly induces both humoral and cellular immune responses against encoded antigens. Pardoll and Beckerieg teach that human growth hormone (hGH) constructs under transcriptional control of either the human β-actin promoter or CMV promoter induced specific anti-hGH antibody responses. The

titer of antibodies was somewhat variable and strain dependent. In addition, clear-cut booster effects of subsequent DNA immunizations were observed, akin to what is typically seen with recombinant protein immunizations (page 167, first column, first paragraph under "Generation of Immune Responses by Naked DNA Vaccines").

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to introduce a expression plasmid comprising the gene encoding *Chlamydia* STK to an animal, in order to invoke an immune response.

One having ordinary skill in the art would have been motivated introduce an expression plasmid comprising the gene encoding *Chlamydia* STK into an animal, in order to obtain a specific immune response to *Chlamydia* STK protein.

There would have been a reasonable expectation of success given the results of Pardoll and Beckerieg demonstrating injection of naked DNA through any number of routes reproducibly induces both humoral and cellular immune responses against encoded antigens. Further Pardoll and Beckerieg teach that a specific antibody response was produced against a hGH construct under transcriptional control of either the human β-actin promoter or CMV promoter.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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JH